Nutmeg as a Narcotic

ANDREW T. WEIL[1]

Introduction

In his search for varied experience and escape from everyday boredom, Man has found many substances of plant origin that poison the human organism but that, at the same time, cause pleasurable physical or mental changes. The word "narcotic" technically refers to a stupor-inducing drug, but it has been applied loosely to many of these deliberately consumed substances. Alcohol, opium, and morphine are narcotics in the strict sense; marihuana, peyote, and psilocybine in the broad sense.

According to Aldous Huxley (1), the ideal narcotic would be

> . . . potent in minute doses and synethesizable . . . less toxic than opium or cocaine, less likely to produce undesirable social consequences than alcohol or barbiturates, less inimical to heart and lungs than the tars and nicotine of cigarettes. And, on the positive side, it should produce changes in consciousness more interesting, more intrinsically valuable than mere sedation or dreaminess, delusions of omnipotence or release from inhibition.

Nothing available today meets all of these specifications. In using his narcotics, Man must tolerate a variety of drawbacks.

Nevertheless, narcotics are used regularly in nearly all parts of the world, and three observations about these practices are relevant to the present paper. First, Man, it seems, is willing to experiment with almost anything in his environment: such bizarre materials as airplane glue, morning-glory seeds, cinnamon, and spider webs have all been put to narcotic use. Second, persons who use narcotics are often willing to suffer extreme discomfort along with the pleasant effects produced by drugs.

Finally, individual reactions to narcotics are profoundly influenced by psychological factors. William James and his friends in Boston after the Civil War found that they could enjoy transcendent insights by inhaling laughing gas. More recently, similar results after sniffing airplane glue have been experienced—an indulgence that does little more on its own than cause dizziness. Apparently, what some narcotic drugs do to the mind is slight compared to what the mind, given a chemical prod, may do on its own.

The use of nutmeg as a narcotic illustrates all three points: nutmeg is an obscure drug, causes many alarming symptoms, and brings about pleasant mental changes only in the proper psychological context. Yet the reason that nutmeg must be considered a narcotic is not only that it can induce stupor but that many persons now deliberately consume it to escape from reality.

Botanical, Historical, and Commercial Notes on Myristica Fragrans

Nutmeg and mace are both products of the nutmeg tree, *Myristica fragrans* Houtt. (Myristicaceae). The genus comprises about 100 species found throughout the tropics, especially in the Malayan region; but of these, *M. fragrans* alone contains enough of an aromatic essential oil to make it valuable for cultivation. Nutmeg is the dried seed of the plant; mace is the dried aril surrounding the shell enclosing the seed.

Many writers have commented on the beauty of the nutmeg tree. It grows usually to a height of 30 or 40 feet, though in its native lands—the Banda Islands and other islands of the East Indian archipelago—it often attains 60 feet, while in Penang it commonly remains a mere shrub (2). The bark is dark gray; the branches are spreading; the leaves are alternate, oblong-ovate, four inches long, leathery, and glossy green above. Normally, the species is dioecious. Flowers, male and female, are shaped like those of the lily-of-the-valley; they are pale yellow, fleshy, and have a strong scent of

---

[1] Vanderbilt 201, Harvard Medical School, 107 Avenue Louis Pasteur, Boston, Mass. Thesis for Honors in Biology, Harvard University.

Received for publication June 25, 1963.

nutmeg. Male flowers are borne in cymes arising near the axils of leaves, but female flowers are either solitary or in groups of three (2). The fruit is a pendulous, fleshy drupe resembling an apricot in form and color (3):

> When quite ripe, the fleshy husk opens by splitting from the top, along the groove, into two halves, nearly to the base. The husk or *pericarp* is of a somewhat firm texture and ½ inch thick, rather acid in taste, with an aromatic flavour of nutmeg. Within the husk is the seed, the nutmeg of commerce, enclosed in a deep brown shining seedcoat, the *testa,* and over this lies a crimson network, the mace, which is an *arillus* or outgrowth from the base of the seed.

The mace is attached to the seed only at the base, and consists of narrow, irregular flaps that closely enwrap the entire testa. Within the shell is the oval nutmeg, usually just under an inch long, woody in texture, strongly aromatic, and oily.

The nutmeg tree requires a hot, humid climate. It is widely cultivated in the tropics, particularly on the Spice Islands (the Moluccas), around the Strait of Malacca, and in the Caribbean (notably on Grenada).

The ancient Greeks and Romans did not know nutmeg and mace (4), but it is likely that Arabian traders were importing Myristica from the East Indies by the first centuries A.D. No definite evidence of nutmeg's appearance in Europe occurs until the end of the 12th Century. In a poem dating from about 1195 and describing the entrance of Emperor Henry VI into Rome before his coronation, Petrus de Ebulo (5) mentions that the streets of the Eternal City were fumigated for the occasion with "Myristica" and other aromatics. Ridley (3) adds that both nutmeg and mace must have been well known in Europe by this time, "for it is recorded that about 1284, 1 lb. of mace cost 4s. 7d., the value then of three sheep, or half as much as a cow."

Nutmeg's true home remained undiscovered for some time. The traveler Masudi, during a visit to India in 916-920, noted (6) that nutmeg, clove sandalwood, and *Areca* came from the "eastern islands." Furthermore, on the way back from his great trip to China (1271-1295), Marco Polo visited the Malayan archipelago (the first European to do so) and listed nutmeg as one of the area's resources (4). Yet, despite these clues, the source of nutmeg was not known in the West until the Portuguese reached Banda in 1512. Portugal controlled trade in nutmeg and mace from that year until the beginning of the 17th Century, when most of the Pacific spice-producing territories fell into the hands of the Dutch. (3).

In a ruthless campaign to keep prices extremely high, the Dutch tried to limit cultivation of the nutmeg tree to the islands of Banda and Amboina. But they were frustrated both by fruit pigeons that carried the seeds to other islands (3), and by the French, who introduced the tree into Mauritius in 1769 (7). The British East India Company, furthermore, sent a representative to the Moluccas in 1796 to collect spice plants, and with his help, nutmeg trees were growing in Penang a few years later (7). Breaking the Dutch monopoly brought prices of nutmeg and mace down to more reasonable levels.

The Spice Islands (now part of Indonesia) have continued to be a center of nutmeg production, along with Penang and other areas in the former British Crown Colony of the Straits Settlements (now part of the Federation of Malaysia). Although *M. fragrans* has been planted in many countries outside the Far East (including some in Africa and South America), its cultivation has been firmly established only in one other area: the West Indies. In 1802, nutmeg trees were smuggled from Cayenne in French Guiana to the British-held island of St. Vincent; thereafter, nutmeg growing spread throughout the Antilles, reaching Grenada, for example, in 1843 (4).

The nutmeg tree is slow-growing, taking 15 years to produce full yields. The fruits mature six months after the flowers fall and are fully ripe when the pericarp splits, revealing the mace-enclosed testa. Exceptional trees may yield more than 10,000 nuts a year; in general, a good tree yields 1500-2000 annually—a weight of ten pounds of nutmeg to one of the mace (4).

The nut, with its mace, is removed from the husk; the aril is then detached from the seed either by hand or with a knife. Fresh arils are brilliant red and leathery, with a strong flavor of turpentine. The mace may be kept in one piece ("double-blade") or separated into two halves ("single-blade"), before it is flattened by hand or between boards. It is then dried thoroughly in the sun or by artificial heat during which process it gradually turns orange, then orange-yellow and acquires its characteristic aroma. Dried mace is packed in teak casks (4).

The nutmegs, usually in their shells, are likewise dried, frequently over a smoudering fire. When completely dry, the seed rattles in the testa. Some nutmegs are exported at this stage. More commonly, the seed is removed after the shell is cracked with a wooden mallet or in a special machine. Sometimes, shelled nutmegs are treated with lime before shipping to protect them from insects. They are then sorted by size and packed (3). For the spice trade, nutmegs are valued according to size, smoothness, light color, and freedom from adulteration with wild seeds.

"Banda mace" is the trade name given to the aril is *M. fragrans*, regardless of where it is grown (3):

> As met with in commerce it is pale orange-brown or brownish yellow, flattened, 1½ to 1¾ in. long, ¾ to 1 in. wide, the forked segments having rounded axils. The tips are usually folded over into a kind of cap. The surface is dull. The flavour like that of nutmeg, but distinct, but there is no acridity.

The finest mace and the finest nutmegs come from Penang, and, in general, the East Indian spices are preferred to the West Indian.

Whole mace is never found in retail stores —only the ground spice is available. Whole nutmegs are much less common than they once were. Not too long ago, the nutmeg-grater was a familiar kitchen item; today, most housewives use ground nutmeg. In the United States, nutmeg and, especially, mace are relatively expensive compared with other popular spices: a 2¾ ounce jar of whole nutmegs (about 15 nuts) sells for $1.25; a 3⅛ ounce jar of East Indian ground mace costs $1.50 (8).

Products of Myristica: Their Uses and Composition

Nutmeg husks. The pericarp of the nutmeg fruit may be preserved in sugar while unripe, salted and dried as a condiment, or made into jellies. All of these preparations have the flavor of nutmeg, and all are reported to be delicious. But they are virtually unknown outside the regions in which the nutmeg tree is grown (3, 4).

Nutmeg. Ground nutmeg, a granular orange-brown powder with characteristic aroma, is a familiar kitchen spice (9):

> It has an aromatic odor and a warm, aromatic, slightly bitter taste. Used in custards, puddings, pumpkins and fruit pies, also gives a delicate flavor to cabbage and as a sprinkling on "egg nog," cauliflower and spinach.

In the past, nutmeg has had wide applications in medicine (see below).

Whole nutmeg, depending on the variety, contains from 5 to 15 per cent of a volatile oil which accounts entirely for the aroma and flavor of the spice. Ground nutmeg is subject to rather rapid losses of this component. In addition, dried nutmegs contain 25 to 40 per cent of fixed oil and 5 to 15 percent ashes. The remainder is moisture, fiber and starch (7):

> The U. S. Definitions and Standards for Food Products require nutmegs to contain not less than 25 per cent of non-volatile ether-soluble extractive matter, not more than 10 per cent of crude fibre, not more than 5 per cent of total ash, nor more than 0.5 per cent of ash insoluble in hydrochloric acid.

Mace: Mace, though not quite so well known in the kitchen as nutmeg, is nevertheless a popular spice. It is a brownish yellow or brownish orange, granular powder with a strong aroma resembling closely but by no means identical to that of nutmeg (11):

> Mace is more favoured for use with savoury dishes, and is employed in the manufacture of pickles, tomato ketchup, etc. In suitable combinations it gives an agreeable smoothness to the flavour. Mace is also especially good in fish pasties, sauces for fish, etc.

In addition, it is used in "pastries, cookies and baked goods, preserves; and adds a delicious flavor to oyster stew and baked fish" (11). Good cooks sometimes add mace to cherry pie and maintain that it is indispensable in making pound cake. Like nutmeg, mace has been used in medicine.

Whole mace contains from 4 to 14 per cent of a volatile oil very similar to that found in nutmegs (10, Vol. V), along with moisture, fat, starch, etc. (7).

> The U. S. Definitions and Standards for Food products require mace to contain not less than 20 per cent nor more than 30 per cent of non-volatile ether-soluble extractive matter, not more than 10 per cent of crude fibre, not more than 3 per cent of total ash, nor more than 0.5 per cent of ash insoluble in hydrochloric acid.

Fixed oil of nutmeg. The fixed oil of nutmegs is known by many names, some of them confusing: nutmeg butter, balsam of nutmegs, oil of mace, butter of mace, banda soap, and *Oleum Myristicae Expressum.* It is obtained by exposing the nuts to hydraulic pressure and heat and is produced normally from nutmegs that are small, broken, worm-eaten, or otherwise unfit for sale. Nutmeg butter has no culinary importance, but it has found applications in medicine and industry and was an item of commerce as early as the end of the 16th Century (4). At room temperatures it is an orange tallowy mass, with a pronounced aroma of nutmeg and the consistency of butter.

Fixed oil of nutmeg has been used in the manufacture of certain soaps, hair tonics, and perfumes. It may still have very limited medical use in external applications for the relief of rheumatism and sprains (3, 4, 7). In 1908, Power and Salway examined the fixed oil and worked out its composition (12):

1.	essential oil	12.5%
2.	trimyristin	73.0%
3.	oleic acid (as glyceride)	3.0%
4.	linolenic acid (as glyceride)	0.5%
5.	formic, acetic, and cerotic acids	very small amounts
6.	unsaponifiable constituents	8.5%
7.	resinous material	2.0%

> The unsaponifiable constituents consisted of a new compound $C_{18}H_{22}O_5$ (amounting to about 5 per cent of the expressed oil), together with some myristicin . . . and a very small amount of a phytosterol, $C_{20}H_{34}O$.

Essential oils of nutmeg and mace. The essential or volatile oils of nutmeg and mace are obtained by steam distillation. In commerce, both products go under the name of "oil of nutmeg" (officially, Myristica Oil or *Oleum Myristicae*), and, in fact, the commercial oil probably is distilled only from nutmegs since they are cheaper than mace. As in the preparation of nutmeg butter, damaged and inferior nuts are used as sources of the oil (10, Vol. V):

> Oil of nutmeg is a mobile, almost colorless or pale yellow liquid, possessing an odor and flavor characteristic of the spice, especially on dilution. With the passage of time, the oil takes up oxygen and partly resinifies becoming more viscous.

Because the oil does not completely reproduce the flavor of whole nutmeg, it is not satisfactory as a substitute for the spice in cooking. ("Essences" of nutmeg and mace sold by spice dealers are alcohol extracts, not essential oils.) But oil of nutmeg has been widely used in industry as a flavoring agent for perfumes and dentifrices and in medicine as a carminative. In fact, it is still official in the United States Pharmacopoeia (13).

East Indian Myristica oil has the following physical constants: specific gravity, 0.880 to 0.910; optical rotation, +8° to +30°; refractive index at 20°C., 1.4740 to 1.4880. On evaporation, it should not leave more than 2.2 per cent of residue. It is soluble in 3 volumes of 90 per cent alcohol (13).

Oil of nutmeg is chemically complex, as one can see from the analysis by Power and Salway (14):

1.	eugenol and isoeugenol	~ 0.2%
2.	*d*-pinene and *d*-camphene	~ 80.0%
3.	dipentene	~ 8.0%
4.	*d*-linalool, *d*-borneol, *i*-terpineol and geraniol	~ 6.0%
5.	small amount of an alcohol, apparently terpineol-4	—
6.	trace of an aldehyde resembling citral	—
7.	safrole	~ 0.6%
8.	myristicin	~ 4.0%
9.	free myristic acid	~ 0.3%
10.	some myristic acid as esters	—
11.	small amounts of formic, acetic, butyric, and octoic acids as esters	—

The "odor and flavor, as well as physico-chemical properties of mace oil, closely resemble those of nutmeg oil" (10, Vol. V).

Myristicin, $C_{11}H_{12}O_3$, is interesting as the fraction responsible for many of the physiological effects of nutmeg and mace (15):

It is a yellowish liquid which boils at 149°C. under a pressure of 15 mm. By prolonged heating with alcoholic potash it is converted into isomyristicin, a crystalline solid melting at 49°C. Either of these substances can be converted by cautious oxidation into myristic aldehyde and finally into myristic acid.

Myristicin occurs in the essential oils of several species other than Myristica, especially in the umbelliferous genera *Anethum* (dill), *Levisticum* (Scotch lovage), *Pastinaca* (parsnip), and *Petroselinum* (parsley). It has also been found in the mint family (genus *Orthodon*) and the Laurel family (*Cinnamomum glanduliferum*) (16).

Chemically, myristicin resembles three other aromatic ether components of Myristica oil: eugenol, isoeugenol, and safrole (Fig. 1).

Until quite recently, both chemists and pharmacologists assumed the "myristicin fraction" of nutmeg oil to be a simple substance (myristicin). In 1963, however, Shulgin (17) showed this assumption to be erroneous. He isomerized the fraction with alcoholic KOH, removed the resulting *trans*-isomyristicin by crystallization, then analyzed the mother liquors by vapor pulse chromatography. Four peaks were observed, three of which turned out to be the expected products of the reaction—methylisoeugenol, *cis*-isomyristicin, and *trans*-isomyristicin. But the fourth was identified as isoelemicin, suggesting the presence of elemicin in the original myristicin fraction (Fig. 1). Shulgin confirmed the suggestion with low temperature chromatography by separating "myristicin" from nutmeg oil into myristicin and elemicin. He then tried to drive off elemicin from the oil fraction by repeated fractional distillation, but so close is the mixture to being azeotropic that he was unable to raise the myristicin content above 70 per cent. "Consequently," he concluded, "in assigning chemical and biological properties to the substance as isolated from nutmeg, allowance must be made for this congeneric contaminant."

History of Nutmeg As a Medicinal Agent

In Arabian medicine. Shortly after Mohammed's appearance, probably in the middle of the 7th Century, a Syrian priest, Aron, mentioned nutmeg in a medical compendium that was soon put into Arabic. Clearly, nutmeg even then had found medicinal application, although just how the spice was first prescribed is not known (4). The earliest exact pharmaceutical reference to nutmeg occurs at the end of the 9th Century in a work of a Bagdad physician, Isaac ibn Amran (4). Warburg writes (4) that, even in this early period, Myristica was recommended for a variety of disorders but was mainly restricted to those of "the digestive organs, from the mouth to the stomach to the intestines, to the liver and spleen, as well as for freckles and skin blotches."

Later Arab physicians referred nutmeg to the class of "warm and dry drugs" and elaborated on its applications. By the 11th Century, for instance, the spice was praised for its effect on the kidneys, was used to combat pain, vomiting, and lymphatic ailments, and was even mentioned as an aphrodisiac (4). According to Ainslie (18, Vol. I), though, the Arabs were using nutmeg almost solely as a hepatic and tonic by the 19th Century. It seems that physicians of the Near East took little notice of mace until the early 1800's, when they began to prescribe it as an aphrodisiac and carminative (4).

At the present time, nutmeg is still important in this part of the world. A pharmacologist at the Hebrew University of Jerusalem writes (19):

> The nutmeg is used by Arabs of Israel and people of its oriental Jewish communities, especially Yemenites, as a drug of their folk medicine, as well as a spice and as an important ingredient in love-potions. It is used against vomiting and to regulate the movements of the bowels; it is good for the liver and for the spleen. It is used in the treatment of TB, against colds, fever and, in general, respiratory ailments. It is said to be an antihelminthic and is used for that purpose mixed with pumpkin or chickpea seeds. It is used against skin diseases, e.g. eczema, scabies, etc. It is said to be effective for removing blotches from the face. To increase *potentia virilis* it is pounded well and added to various foods.

In Indian medicine. Frequent references in the Vedas to nutmeg indicate that the ancient Hindus knew of the spice from early times. It was described by them as warmth-producing, stimulating, good for digestion,

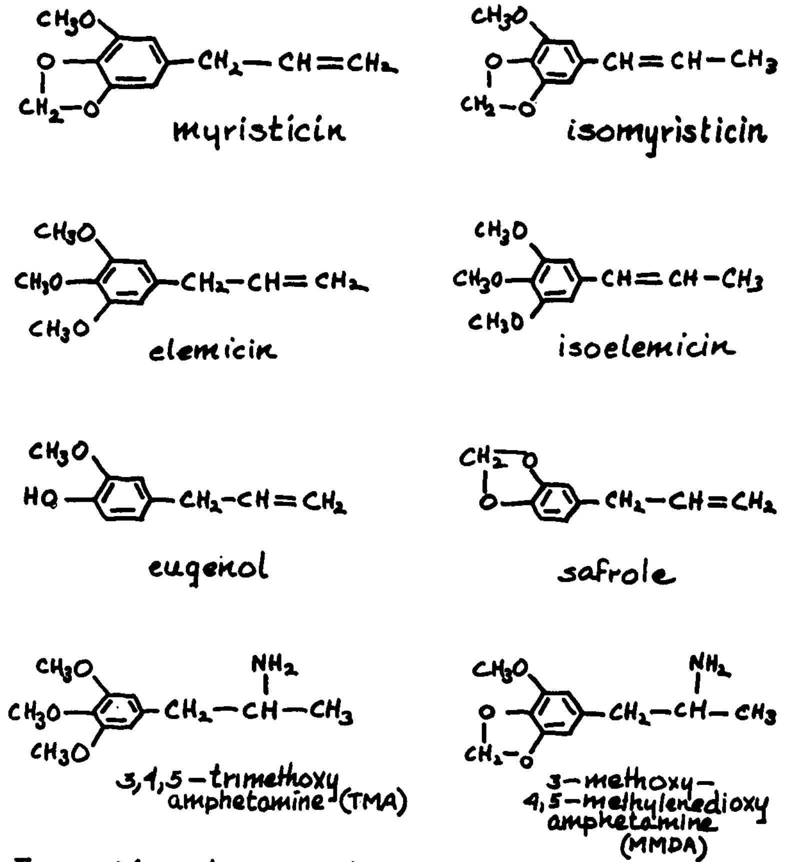
myristicin
isomyristicin
elemicin
isoelemicin
eugenol
safrole
3,4,5-trimethoxy amphetamine (TMA)
3-methoxy-4,5-methylenedioxy amphetamine (MMDA)

Fig 1. Myristicin and Some of its Chemical Relations.

and it also figured in their medicinal preparations. Martius (20) says that Hindu physicians prescribed it for headache, nerve fevers, cold fevers, foul breath, and intestinal weakness.

Presumably, these uses continued, for Ainslie (18, Vol. I) in his *Materia Indica* of 1826, writes that nutmeg "is considered by the natives of India as one of their most valuable medicines in dyspeptic complaints, and in all cases requiring cardiacs, and corroborants; they likewise prescribe it to such puny children as appear to suffer from weaning." He adds that Indian physicians administer mace in cases of fever, consumption, chronic intestinal disorders, and asthma. Later commentators confirm Ainslie's observations and add to the list toothache, dysentery in children, cholera, swellings of internal organs, flatulence, liver and spleen congestion, and rheumatism (4). Dymock, in 1883, is the first to mention an aphrodisiac use of nutmeg outside the Near East. He says (21) that the Moslems of western India use the spice in this way in addition to incorporating it into their remedies. Burkill, writing in 1935 (22, Vol. II), stresses nutmeg's importance in Indian tonics for dysentery and mentions further that the *Medical Book of Malayan Medicine* employs the spice for madness as well as for the usual digestive ailments. According to an adviser in the Indian Ministry of Health, nutmeg is still widely used in Indian medicine (23):

> It is prescribed as an analgesic in neuritic pains, as a sedative in highly tense nervous

states, and as a sedative and antispasmodic in asthma. In view of its reaction resembling opium, it is used to give relief in the cough and hemoptysis of tuberculosis. In traditional Indian folk and domestic medicine, nutmeg is used in small quantities to induce hypnotic effect in irritable children. It is also administered as an hypnotic and sedative in epileptic convulsions.

In Western medicine. Medieval European physicians followed exactly the precepts of Arabian medicine. So it is that we find an 11th Century Greek physician, Simeon Seth, calling nutmeg a warm, dry drug and recommending it for the same range of maladies. His only original contribution is his prescription of the spice for pulmonary disorders (4). Warburg writes (4) that:

> The importance of nutmeg as a medicine grew hand in hand with the increase in Indian trade during the middle ages; its use spread from the Arabian empire over Greece and Italy and soon reached central Europe. Nutmeg gradually became a genuine folk remedy, although it was most important as a major ingredient in medicines prepared according to guild rules.

Western physicians of the 16th and 17th Centuries merely compiled the writings of earlier authorities on nutmeg. This was the great period of the herbalists, however, and nearly every herbal contained a summary of nutmeg's virtues. The following passage on "Nux moschata" from Parkinson's *Theatrum Botanicum* of 1640 (24) is typical:

> They [nutmegs] are used in all the cold griefes of the head or braine, for palsies, the shrinking of sinewes, and the diseases of the mother, they are hot and dry in the second degree, and are somewhat astringent, serving to stay the laske, they cause a sweet breath and amend a stincking, they helpe to discusse winde, either in the stomache or bowels, it helpeth to quicken the sight, and to comfort the spirits, and provoke urine, and are comfortable to the stomacke, and helpe those that are feeble or macilent to grow fat as also helpeth Venery and increaseth sperme, they help to procure rest and sleepe by allaying the distemper of the spirits, being applyed to the temples. The Macis are of the same property, but somewhat more warming and comforting, the thicke oyle that is drawne both from Macis and Nutmegges, are either of them of good use in pectorall griefes to warme a cold stomacke, and the cough, and to dry up rheumaticke destillations of cold flegme thereunto or upon the lungs. The chimicall oyle of either is of more efficacy both for pectorall and cephaticall diseases, but must be cauteously [*sic*] and sparingly used.

An amazing book of the time was *De nuce moschata* or *Moschocaryologia* of J. H. Dietz—a 60-page dissertation on nutmeg, published in 1681. It is important as the first truly systematic treatment of Myristica's applications in medicine, though Dietz lists so many of these that nutmeg is held to be a virtual panacea. In 1704, Dietz's compendium was surpassed by a 900-page monograph on nutmeg—the *Moschocaryographia seu Nucis moschatae curiosae descriptio* of C. F. Paullini. Paullini includes a wealth of historical and cultural material as well as pharmaceutical data. Like Dietz, he considers nutmeg a cure-all, recommending its use in the treatment of no fewer than 138 diseases (4). Later treatises on nutmeg and mace followed Paullini, and not until near the end of the 18th Century did Myristica begin to lose the high reputation it gained as a result of all these articles. Warburg (4) has accurately termed the 1700's the "high point of the medicinal use of nutmeg."

Doctors continued for some time to prescribe Myristica for intestinal illnesses, but by 1800 they began to realize that many of its effects were the same as those of other aromatics. Then, as modern pharmacy developed, older remedies, nutmeg among them, were relegated to positions of lower and lower priority. In summarizing the medicinal uses of the spice in 1897, Warburg writes (4):

> Today the employment of nutmeg and mace in medicine is relatively minor. Nutmeg is now used as a stomachic, stimulant, and carminative, especially in cases of dyspepsia, intestinal catarrh, and colic, and as an appetite stimulant, as well as for its ability to control flatulence. . . .

There is an important omission in the above catalog of nutmeg uses: sometime late in its history—perhaps as late as the 19th Century—nutmeg became known as an emmenagogue and abortifacient. Presumably, folk medicine alone contributed this application, for none of the early scientific papers attribute any abortion-inducing properties to Myristica. No one has explained the ori-

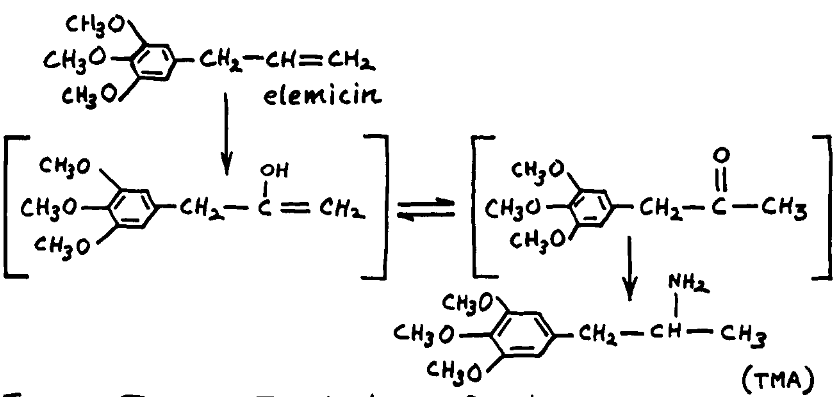

Fig 2a Possible Production of a known Psychotomimetic Agent from Elemicin

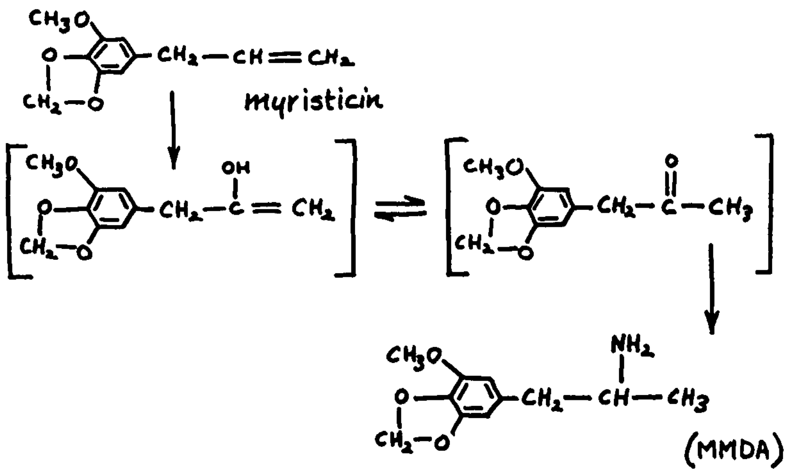

Fig 2b Possible Production of a known Psychotomimetic Agent from Myristicin—

gin of the belief, which seems to have been confined to western Europe and North America; and, more puzzling still, many early commentators praise nutmeg's ability to *prevent* miscarriage. (See, for example, Blackwell's *A Curious Herbal*, London: 1739, Vol. II, *plate 353*, p. 89; Dietz, for one, specifically prescribes it against possible abortion.) All that Warburg can add is that "the emmenagogic, menstruation-promoting effects which have been attributed to it in folk medicine seem very dubious; it appears that nutmeg is still used abundantly to produce abortion by women in England and America, but mostly with negative results"(4).

This idea has persisted among women into the present century; indeed, Green (25), in 1959, reported the case of a 28-year-old Virginia woman who ate "18.3 Gm. of finely ground nutmeg in an attempt to induce the menses, which had been delayed two days." Some of the older uses of the drug may also be alive in contemporary folk beliefs: McCord (26), for example, cited a 1962 incident in which a 41-year-old South Carolina man, on the advice of a friend, took two whole nutmegs to relieve a skin infection. McCord also refers to old wives tales about the spice "describing its ability to induce abortion and to cure boils and various other conditions."

Myristica remained official in the United States Pharmacopoeia through U.S.P. XIII, and Myristica Oil is still included in the current edition (U.S.P. XV-1955). The oil is retained primarily as a flavoring agent, but the 25th edition of the *Dispensatory of the United States of America* (1955) designates it also as a "carminative and as a local stimulant to the gastrointestinal tract" (27).

The relevance of nutmeg in medicine to the central topic of the present paper is that the toxic properties of Myristica must have been noticed when patients using the substance accidentally took overdoses of the drug.

Nutmeg Poisoning

Early reports. A number of early European physicians described the symptoms of nutmeg poisoning; however, it is difficult to sort out these references, since a few primary observations of toxicity crop up repeatedly in later articles, often much changed. In modern reference works, the evidence of early commentators is often reduced to the sort of statement that appears in *The Wealth of India* with no amplification (28): "Excessive doses of nutmeg have a narcotic effect; symptoms of delirium and epileptic convulsions appear after 1–6 hours."

The first clear mention of the stupor-inducing action of Myristica occurs in the *Plantarum seu stirpium historia* of Lobelius, published in 1576. As one of his observations, the author writes: "Memini generosam Anglam gravidam esu 10 aut 12 nucum myristicarum ebriam delirasse."[2] (4) A second reference is found in *De Medicina Indorum* (1642) of Bontius. He says that nutmegs are seldom eaten because the "oil-rich and fatty fumes" of the seeds rise to the brain where they cause blockages and produce somnolence and stupefaction. "What is worse," he continues, "excessive use of the nut has endangered several persons: they remained motionless and unconscious for more than a day with clear indications that the whole nervous system had been seriously affected" (29, Vol. IV).

In the same century, Rumphius collected a number of accounts of serious consequences attending the ingestion of large amounts of nutmeg. He related the following incidents (4):

1. In 1665, some Germans ate a cold soup of the usual beer and wine in which, according to their statement, they had put nothing other than sugar and seven or eight grated nutmegs. The next day, they suffered acute respiratory distress, feeling as if they were about to suffocate. Their mouths became very dry, their lips swelled, and their heads felt "heavy and giddy." In addition, they became seriously constipated. 2. Two soldiers in Manipa (in the Banda Islands) slept the whole night under a nutmeg tree and woke up with such hangovers that they seemed to be drunk. 3. In 1650, two other soldiers in the Banda Islands became confused and half insane after eating five nutmegs. 4. In 1657, a woman was found dead in her bed with a basket full of nutmegs in front of her. It was concluded that she had eaten so many of the seeds that she sank into a fatal stupor.

These anecdotes of Rumphius are secondhand and open to criticism. The second is especially dubious. Probably, the soldiers used the nutmeg tree to cover up the effects of a drunken spree. Yet, there is so much of this anecdotal material that, considered in its entirety, it makes a convincing case. Another example is this interesting recipe from a 14th Century pharmacopoeia in Middle High German: "Wultu enen vordrynken, nym ene verssche gude muscaten, snyd de mydden unttwe unde gif eme de helfte ethen; darna gif eme de anderen helfte ethen, unde gif eme echter hastichliken drinken, so wert he drunken."[3] (30)

In 1789, the English physician, William Cullen, described (31, Vol. II) a case of Myristica poisoning from his own experience:

---

[2] I remembered a pregnant English lady who, having eaten 10 or 12 nutmegs, became deliriously inebriated.

[3] If you wish to get someone drunk, take a good fresh nutmeg, cut it in half through the middle, and give him one of the halves to eat; then give him the other half to eat and make him take a quick drink. In this way he will become drunk.

> I have myself had an accidental occasion of observing its [nutmeg's] soporific and stupefying power. A person by mistake took two drams or a little more of powdered nutmeg; he felt it warm in his stomach, without any uneasiness; but in about an hour after he had taken it, he was seized with a drowsiness, which gradually increased to a complete stupor and insensibility; and not long after he was found fallen from his chair, lying on the floor of his chamber in the state mentioned. Being laid abed he fell asleep; but waking a little from time to time, he was quite delirious: and he thus continued alternately sleeping and delirious for several hours. By degrees, however, both these symptoms gradually diminished, so that in about six hours from the time of taking the nutmeg he was pretty well recovered from both. Although he still complained of headache and some drowsiness, he slept naturally and quietly through the following night, and next day was quite in his ordinary health.
>
> There is no doubt that this was entirely the effect of the nutmeg. . . .

Ainslie (18, Vol. I) writes that "nutmeg, like mace, taken in large quantity, is apt to produce stupor and drowsiness" and points out that Hindu physicians are therefore cautious in using both spices.

The great physiologist, J. E. Purkinje, conducted self-experiments with nutmeg in 1829 (32). For his first test, Purkinje ate one whole nut with sugar. He felt a weariness and depression for the whole day without mental disturbances and decided to try a larger dose the next time; subsequently, he ate three nutmegs on one afternoon. Shortly thereafter, he experienced marked drowsiness interrupted by pleasant dreams and some restlessness. His own description of later effects (33) is significant, because it is quite unlike the accounts one finds in most articles and strikingly similar to descriptions of *Cannabis* intoxication:

> At half-past six, when it was almost dark, I woke up in order to go to the Royal Theater at Brueder Street where I lived. The distance was long, but this time I thought it had *no end.* My movements appeared entirely adequate, but were lost momentarily in dream pictures, from which I had to extricate myself with considerable force in order to keep on walking. My feet did their duty and, since I had to stick to a straight road, there was no danger of going astray. I went forward in this dream, for, if I attempted to orient myself, I could not even recognize the cross streets. Time seemed long, but I got to the opposite side of the place where I was going. During this time dreams and physical activity battled one another. The return journey was good, and I slept well that night and next day.

In 1841, Endlicher listed the symptoms of Myristica poisoning as pressure in the chest, heavy breathing, intense thirst, headache, inebriation, and even delirium and "fatal apoplexy" (34). Pereira (1850) cited a new case in which two drams of powdered nutmeg caused somnolence deepening to complete stupor (35). Warburg mentions (4) another case, reported in the British Medical Journal, of ingestion of one nutmeg as a cure for diarrhea—even this amount was enough to cause giddiness and drowsiness lasting until the next day. He also says that Ten Bosch, in 1865, described severe poisoning from eating seven seeds, and he mentions an incident in Florida where consumption of one and one-half nutmegs produced, within an hour, insomnia, which, in another hour, passed first into stupor, afterwards into excitement, headache, laughing fits, and fantasies, followed by collapse. On the other hand, Warburg reports (4) that Fronmueller, in the course of experiments on sedatives, gave people two large nutmegs and observed buzzing in the head as the only symptom.

Poisoning by mace is never mentioned in the literature, with one notable exception. G. C. Watson, in 1848, published a dramatic account of mace intoxication (36), one that most later commentators, including Warburg, have missed and that, like Purkinje's observations, does not conform to the usual pattern of general physical excitement followed by stupor. Watson quotes the patient's own description:

> At about eleven o'clock in the forenoon of the 12th of March, 1847, I was in a sale-room in which there were samples of spices &c.; and from curiosity, I ate about as much mace as could be lifted on a teaspoon, if broken small. About half-past twelve o'clock I felt a pain on the crown on the head, extending over a space about the size of a penny piece; I also felt a slight nausea of the stomach, as if I had been smoking inordinately. I had kept eating the mace in small bits over about an hour and a half. I walked home and dined about three o'clock. I still felt the pain slightly on the top of my head, and also the nausea and slight gid-

diness. I rose from dinner and looked out at the window, to dissipate, if possible, this disagreeable feeling. I then felt the blood rush to my head, but the feeling was as if an electric current had passed from the crown of my head downwards. Not wishing to be overcome in the room in which I then was, I made an effort, and got mechanically down-stairs. I then felt the same sensation which I suppose a person would experience who had become nearly insensible from extreme cold, and that if I had yielded myself to its influence, I could have slept away existence without pain. I felt this sensation twice; the second time when I had got down stairs into the back parlour. I then walked about in the back yard, to endeavour to drive away the extraordinary sensations, but in a few minutes a cold shiver came upon me. I then got into the house, and laid myself upon a sofa near the fire.

From that time I felt every variety of heat and cold from their respective extremes. At every time the blood went and returned from my head, the current changed the sensation, sometimes feeling myself very hot, and the next very cold, but never the same sensation. I felt at one time such a pressure in the head, that it appeared as if all the blood in the body had rushed to obtain possession of that region, and I thought I could hear it gushing in my ears. These symptoms became gradually weaker.

A medical gentleman was hurriedly called in and some brandy was administered. The effect of this upon me was as if I had been electrified from the roof of the mouth downwards in a straight line, and dying off towards the feet; it then seemed to diffuse itself over the whole body. The state of my body generally felt as if I had hold of slightly galvanized wires, the wires apparently working in antagonist directions, out of tune and keeping;—like in fact, so many connecting rods working from excentrics out of truth, and jarring against each other. The state of the mind was, I should suppose, similar to that of the opium eater, entertaining no apprehension of the result, although aware of the presence of some danger.

Watson remarks on the persistence of this mental disturbance: three days later, the bizarre state of consciousness had still not abated entirely, and the man's thoughts "hardly submitted themselves to his control, unless by a consciously great effort."

Wide use of Myristica as a remedy in the Far East would lead one to expect numerous cases of poisoning in that part of the world, but, oddly, no reports on any such mishaps seem to occur in the literature, and it is not possible to trace to its source the inadequate statement in the 19th edition of the *Dispensatory of the United States of America* (37):

> Nutmeg unites to the medicinal properties of the ordinary aromatics considerable narcotic power. In the quantity of two or three drachms (7.7 or 11.6 Gm), it has been known to produce stupor and delirium, and dangerous if not fatal consequences are said to have followed its free use in India.

Intoxication following the use of nutmeg as an emmenagogue or abortifiacient. By far the greatest numbers of people poisoned by nutmeg have been women—mostly English and American women in the late 19th and early 20th Centuries—who took the spice in efforts to bring on menstruation or induce abortion. A great many of these cases appear in the literature of the period, particularly in British medical journals. Commenting on them in 1962 McCord observes (26):

> It is interesting that of all the instances reviewed in which nutmeg was taken as an abortifacient, this effort was successful in only one patient. Even in this instance the role of nutmeg was open to question since the abortion followed the ingestion by a period of a month.

Examples of this sort of poisoning are too numerous and too repetitive to warrant a complete inventory. Selected cases give a good clinical picture:

In 1881, Hammond (38) published an account referring to a woman who took one and one-half powdered nutmegs in half a glass of hot water. Two hours later, she had violent stomach pains followed by headache: then consciousness was lost for six hours. Eventually, she vomited and, after twelve hours, recovered. In a similar instance (4) a woman took three nutmegs and devloped stomach pains and nausea in two hours. After another hour, she lost consciousness and remained unconscious for eight hours with weak pulse, slow breathing, elevated temperature, protruding eyes, dilated pupils, cold extremities, cyanotic lips and nails, and flaccid sphincter muscles of the bladder and intestine.

The American physician, P. J. Farnsworth, in 1904, reported some of his observations on nutmeg (which, he says, in large quantity "is like an overdose of Chloral without any of the depressing symptoms") (39):

> Some years ago I was called in the evening to see a young married lady who was visiting some wealthy friends in the country. About noon she had been discovered in a profound sleep, from which they were unable to arouse her. Her respirations were natural, her pulse soft and a little slow, pupils a little dilated but responsive to light, skin moist, extremities rather cool. I could get no history of accident or previous illness, and directing them to watch her and report any change, I concluded to wait further developments. The sleep continued well into the next day, when she was aroused with no other feeling than languor from so protracted sleep.
>
> She said she had gone a few days over her "period" and was told that nutmeg was a good remedy to bring it on. That she also had a "looseness" of the bowels. She grated into a spoonful of brandy three (3) medium sized nutmegs, that it had a pleasant taste and she ate the whole, and soon after fell asleep. Her menstruation returned and the diarrhoea was checked and she felt no other inconvenience.

During a discussion of a paper on nutmeg at the Royal Society of Medicine in 1909, some additional facts emerged (40):

> J. Gray Duncanson said that people in this country [England] did not take nutmeg to cause death but to produce abortion. . . . Nutmeg was somewhat frequently taken by women especially in the neighbourhood of London, to bring on a miscarriage, but as it was done surreptitiously it was very difficult for the medical man to ascertain in what form and in what quantity it was taken. Those cases which he had seen had been marked by gastro-intestinal disturbance, and it was difficult to know whether to attribute that to the nutmeg entirely, or in part to the gin with which it was most frequently administered. In one case which he saw some years ago there were certainly cerebral symptoms—hallucinations and delusions.

Beck, in 1914, reported (41) the cases of two women who took two ground nutmegs mixed with wine, hoping to bring about miscarriage. They experienced dyspnea, some loss of memory, and drowsiness. Both were found unconscious with weak, rapid pulses; both recovered in three to five days.

There are many other reports (42). Summarizing all these data, McCord writes (26):

> . . . patients have consumed from 1 to 3 nutmegs and have experienced restlessness, dizziness, fear of death, coldness of extremities, occasional nausea and vomiting, abdominal pain, and precordial pain or oppression. These patients were found to be extremely agitated, delirous, and dyspneic and have had weak, rapid pulses and decreased body temperature. On several occasions patients were found unconscious. Occasionally there was flushing of the face while at other times pallor with cyanosis of the lips and nails predominated.

He attributes these intoxications to "a central nervous system depressive effect with periods of stimulation and associated respiratory and cardiovascular difficulties. Occasional case reports have suggested a possible hypersensitivity reaction as illustrated by the presence of facial and periorbital edema with flushing."

Other cases and recent cases. Occasionally, Myristica intoxication occurs in children who have accidentally eaten a quantity of nutmeg; if a stupor results, it may be serious. In fact, the only fatality ever attributed to the spice occurred when an eight-year-old boy ate two whole nutmegs, became comatose, and died less than 24 hours later (43). Farnsworth mentions (39) another eight-year-old poisoned by one nut: "Sleep continued through the day with some jerky breathing and some convulsive twitching.... The child came out of it all right."

G. Mendelsohn relates (44) the incident of a man who took "2 to 3 pieces of ground nutmeg" in order to clear up "eczema associated with varicose veins." Consequences included dyspnea, dryness of the mouth, loss of memory, and deep sleep with recovery the following day.

The apparent "epidemic" of nutmeg poisoning around the turn of the century subsided after the First World War. Cases since then have been rare. Green's 1959 report (25) on a 28-year-old woman, who attempted to bring on menstruation with 18.3 g of ground nutmeg, includes the usual physical symptoms as well as profound mental changes which came on eight hours later:

> She had then become completely disoriented, with episodes of wild screaming and purposeless thrashing of the arms and legs. Coordination appeared absent. Interspersed with the disorientation were brief moments of lucidity during which she seemed to be aware of her surroundings. From the time of her awakening at 5:30 a.m. until 9:30 a.m., when she was

> seen by her local physician, there were three intervals of lucidity, each lasting about 10 minutes. The rest of this time she was delirous and in a state of excitement and agitation. . . .
>
> The patient remained in a semistupor for 12 hours after her admission. She then began to experience episodes of wild excitement, with loud screaming and manifestations of a fear of impending death. She continued to be subjected to episodes of excitement for two hours, during which time restraints were needed. For the remainder of the second day she was restless but essentially quiet. During the third and fourth days of hospitalization she slept much but complained constantly, while awake, of a generalized feeling of numbness and dizziness.

Effects of the toxin continued with decreasing severity through the sixth day.

McCord's case in 1962 (26)—the 41-year-old man who ate two nutmegs to alleviate a skin infection—included such symptoms as increased perspiration, dryness of the mouth, drowsiness, weakness, frequent attacks of rapid breathing and "vague, fleeting pains in the chest and left arm," and a pronounced feeling of impending death. According to Payne (45) two college students (19 and 20 years old) had similar experiences in 1963 after each had ingested two tablespoonfuls (about 14 g or the equivalent of two whole seeds) of powdered nutmeg suspended in milk. About five hours later ". . . each had the onset of a significant pharmacologic effect, heralded by a leaden feeling in the extremities and a nonchalant, detached mental state dscribed as 'unreal' or 'dreamlike.' Rapid heart rates and palpitation were noted, and both complained of dry mouth and thirst. Onlookers observed that one student became quite hyperactive and agitated, and talked incoherently. It was noted that the faces of both were 'as red as beets.' Nausea, vomiting, and abdominal cramps were absent. . . . One described a sense of impending doom, as if he were 'breaking up inside.' "

Extreme drowsiness occurred about seven hours after these symptoms began and continued for the next 24 hours. Recovery was complete, but "both patients stated emphatically that a sense of unreality persisted for 48 to 60 hours from the time of 1 oral dose of nutmeg."

Ample evidence, then, is available on the toxic effects of nutmeg and mace. A puzzling feature of this evidence is its inconsistency; there seems to be no agreement on what symptoms characterize the intoxication or on what doses produce it.

Pharmacology of Nutmeg

Before 1910. As a historical curiosity, it might be mentioned that the first pharmacological experiments on nutmeg were performed by van Leeuwenhoek, the Dutch microscopist, around 1676. He exposed mites in a glass tube to pieces of nutmeg and observed that they would first approach the nutmeg and then rebound as they moved closer. If they stayed too close too long they died (32). Despite this noble beginning, and despite all the indications that Myristica was an important cause of poisonings, the pharmacology of nutmeg was neglected for many years.

As late as 1900, little was known about the action of Myristica, largely because researchers could not agree on which component of the seed contained the active principle: essential oil, fixed oil, or endosperm. Although many investigators correctly attributed the narcotic properties to a fraction of the essential oil, a number of writers, Warburg among them, refused to accept this conclusion (4). Warburg, himself, believed a "resin" to be accessory to the oil and expressed regret that experiments (up to 1897) had examined only effects of the oil, which he writes (4), "like all essential oils, is toxic in itself, but which apparently is not present in sufficient quantity to account for the poisonous effects of such small doses of nutmeg (e.g., 6 to 8 g or one and one-half seeds)."

But Frosch had demonstrated, before 1850, that 0.03 g of oil of mace exerted a paralytic effect (4), and, in 1848, Mitscherlich (46) found that 8 g of oil of nutmeg killed a rabbit in 5 days, while 24 g were lethal in 13 hours. Four grams of nutmeg oil killed small rabbits in 30 hours, and even one gram made them sick for several days. Mitscherlich judged these effects to be as strong as those of oil of cinnamon but weaker than those of oil of bitter almonds. Post-mortem examinations revealed "changes in the stomach and small intestine similar to those produced by cinnamon oil and other essential oils: there were blood blisters in the mucous membrane of the stomach; the epithelium of the small intestine had been torn off and turned to mucus; but the colon showed no peculiarities."

Had such reports become well known, they might have hastened the development of knowledge on nutmeg poisoning. As it was, further data were not forthcoming until 1903, when G. B. Wallace published the results of his studies. By that time, the chemistry of Myristica had been investigated, and the findings, which Cushny has summarized, were helpful (43):

> The nutmeg contains from 3 to 8 per cent of volatile oil, and when this has been extracted from it the residue produces no effect whatever on animals, while small doses of the oil itself induce characteristic effects. The oil contains several terpenes and small quantities of higher boiling substances which can be separated by fractional distillation. The terpenes are devoid of action, except in enormous quantities, while the fraction boiling at 150°C at 14 mm. pressure proved to be a powerful poison.

The poisonous fraction was named "myristicin," and Wallace (47) was the first person to test this pure principle in animal experiments. He found that frogs, placed in a dilute aqueous solution of myristicin, showed initial restlessness, followed by depression and complete paralysis. Death ensued if the animals were not removed from the solution. Similar effects followed injection of the solution into the lymph sacs. Wallace showed the action to be confined to the nervous system, with no effect on muscles; the heart, for example, kept beating normally, even when bathed with the solution. Wallace observed similar reactions in rabbits, with ultimate death from respiratory failure. He further noted that the cat was much more susceptible than other animals to the toxic action of myristicin.

In 1904, F. Jurss reported (48) experiments in which he had given myristicin to frogs, fish, birds, and mammals, particularly guinea pigs and rabbits. Jurss calls attention to a puzzling fact when he writes: "The oils of nutmeg and mace only cause fatal poisoning in a rabbit in doses of 10.0 to 12.0 grammes, whereas a single nutmeg (4.0 to 5.0 grammes) is capable of producing in man serious effects." Jurss concluded from this that the oil was more poisonous for man than for animals. Power and Salway, however, point out (49) that the "essential oil of nutmeg is very variable in character, and that some specimens may be practically free from myristicin . . ." Jurss used subcutaneous injections of myristicin (2 cc to 6 cc per kilo of body weight for guinea pigs and 0.9 cc to 1.76 cc per kilo of body weight for rabbits) and found paralysis of the central nervous system followed by death without convulsions. Extensive degenerative changes of the liver were seen in post-mortem examinations.

Sir Henry Dale's investigations of 1909 (40) confirmed Jurss's finding of advanced fatty degeneration of the liver in all cases of death from myristicin. Dale also attacked the question of how the symptoms in animals differed from those in man. Cushny had written (43): "Animals . . . correspond very closely to man in their reactions to nutmeg poison," but Dale showed that this was not so. In man, ingestion of one or more nutmegs causes narcosis varied by excitement and delirium, with recovery after 24 hours. In Dale's words: "The general impression given by most of the clinical records is of a temporary intoxication, which usually passes off without leaving any obvious bad result. . . . On the other hand, I found that the smallest dose of nutmeg, which would produce in a cat any recognizable effect, invariably produced death. . . ." Thus Dale observed that doses smaller than 5 g did not affect the cat, but he cites a case in which a cat weighing 2640 g was given exactly 5 g of grated nutmeg by mouth, which killed it in 48 hours. In the cat, one sees "a uniformly fatal coma appearing after a few days, always associated with, and probably secondary to degenerative liver changes. . . ." (40). The temporary effects in man appear with relatively much smaller doses.

Dale analyzed his observations correctly (40):

> The primary effects on the nervous system, when produced in the cat, are, indeed, closely similar to those observed in man. But, whereas man is so sensitive to the primary action of myristicin that he can be temporarily narcotized by doses of nutmeg too small to leave any permanent bad effects, the nervous system of the cat is relatively so little responsive that doses considerably in excess of that which will

> certainly kill the cat are necessary if the primary effects, as seen in man, are to be reproduced. The death of the cat is in any case, due to secondary coma. . . . The secondary coma I regard as an entirely different phenomenon from the primary action on the nervous system. . . .

A perplexing characteristic of nutmeg poisoning is that pure myristicin, in order to cause the primary symptoms, has to be taken in amounts exceeding those found in normally toxic doses of whole nutmeg. This led some researchers to conclude that myristicin was not entirely responsible for the narcotic effect of Myristica. Dale showed that the results one got with chemically pure myristicin in experimental animals were qualitatively identical to those obtained with nutmeg, but that "the dose given must be proportionately larger." His conclusion, however, is that "the difference in doses may with great probability be attributed to the readier absorption of myristicin when it is associated with the fats and other constituents of the whole drug."

Power and Salway took up the investigation after Dale's study. In a paper of 1908 (49), "Chemical Examination and Physiological Action of Nutmeg," these two authors explore the possibility that the narcotic properties of nutmeg may be due to something other than myristicin. They first carried out special assays for alkaloids or soluble proteins and got negative results. Next, they ran exhaustive tests of the essential oil, the fixed oil, and the press-cake remaining after removal of the fat.

Power and Salway observed what Dale had: that quantities of myristicin in excess of those found in toxic amounts of nutmeg (i.e., toxic to cats) had no apparent effect when given to the cat. On the other hand, none of the other components of nutmeg tested showed any physiological activity. The authors conclude:

> It would be quite reasonable to attribute all the effects of nutmeg on the cat to myristicin, but for the fact that the dose of nutmeg sufficient to cause death in a few days represents a quantity of myristicin which, given by the mouth, produces no appreciable effect. It seems possible however, that the discrepancy may be explained by a consideration of the conditions of absorption. Thus the failure to obtain an effect with small doses of myristicin may be due to its being only imperfectly absorbed when given in a pure state, and passing out to a large extent in the feces.

If this were so, a small dose of myristicin would be more effective if injected subcutaneously in order to ensure slow, continuous absorption. And, in fact, a dose of about 0.12 cc injected subcutaneously in the cat causes "a very slow but ultimately extensive degeneration of the liver . . . ," while up to 0.2 cc has no effects when given orally (49).

The final statement of Power and Salway seemed to settle the problem (49):

> . . . there would appear to be no doubt that the narcotic property of nutmeg is correctly attributed to myristicin . . . and it may be assumed that the latter substance when associated with the other constituents of the nutmeg is in a condition much more favorable for absorption than when in a pure state. As in the case of many other narcotics, the lower animals are much less sensitive than man to the direct action of nutmeg on the cerebral functions.

Recent studies. Pharmacologists did not re-open investigations into Myristica until more than 50 years after Power and Salway published their findings. In 1961, Truitt et. al. conducted a study to determine the safety of nutmeg in man. "In humans," the authors write (50), "the ingestion of one or two ounces of ground nutmeg appears to produce a prolonged period of delirium, disorientation, and a syndrome comparable to alcoholic inebriety."

Truitt and his co-workers first tested the effects of 400 mg of pure myristicin on ten subjects, four of whom had definite reactions to the compound (50):

> These reactions ranged from a feeling of euphoria and restlessness to weakness, nervousness, tremor, and anxiety, tachycardia, gastrointestinal discomfort and nausea. One of the experimenters ingested 15 gms. of nutmeg in acacia suspension. Reaction started in one to two hours, and effects did not disappear until approximately 36 hours after ingestion. Symptoms were marked by vasomotor instability, tachycardia, hypothermia, absolute absence of saliva, constricted pupils, some emotional lability, and a tremendous feeling of isolation and inability to carry or intellectual processes.

Because the reactions to myristicin did not include all of the symptoms produced by whole nutmeg, the investigators thought that other substances in the seed might be pharmacologically active. Accordingly, they tested the effects of 10 mg doses of nutmeg from which all volatile constituents had been removed and found that these produced none of the psychopharmacologic effects of the whole drug but did yield, in some instances, "the undesirable side effects of occasional flushing, lower intestinal discomfort, and unusually heavy sleep or insomnia." "This suggests to the authors," they conclude (51) "that other volatile constituents (safrol, borneol, linalool, eugenol, isoeugenol, and geraniol) in nutmeg contribute markedly to its psychopharmacologic effect in man," and (50) "that myristicin does not reproduce the entire activities of whole nutmeg"—conclusions opposed to those of Power and Salway.

In reviewing the findings of Truitt's group, Shulgin, in 1963 (52), speculates on their theory. He says that the myristicin fraction of nutmeg oil "is strongly suspect of representing the effective toxic factor for cats. . . ." but that it appears "ineffective in duplicating the psychological effects of total nutmeg in man." He then goes on to consider possible pharmacological activity of other components of the oil:

> The minor aromatic ethers, eugenol and safrol, have been suggested as possible active components. This seems unlikely, as the amounts ingested from a 5 g nutmeg (0.001 g and 0.003 g resp.) are much below the usual therapeutic levels of these substances (3.0 ml and 0.5 ml. resp.). The only component, aside from the myristicin fraction, of the volatile oils from nutmeg that deserves serious consideration as an active agent, is the pinene-dipentene fraction. Many descriptions of the toxic syndromes of representative terpene medicines parallel the common toxic manifestations of nutmeg (i.e., nausea, cyanosis stupor, cold extremities, often delirium). [However] Actual toxic dosages of oils that are of make-up similar to the hydrocarbon fraction of nutmeg (as oil of turpentine) are as a rule 20 to 60 times higher than that which would be encountered in nutmeg intoxication.

It is Shulgin's conclusion (52), not Power and Salway's, which now seems incontestable: "As yet, no known pharmacology of any known component of oil of nutmeg can explain the syndrome of the whole nutmeg."

Evidence of Narcotic Uses of Myristica Fragrans

Persistence of rumors. Only one genus in the family *Myristicaceae* is definitely known to be used as a narcotic. It is not *Myristica,* but *Virola*—several species of South American trees, the barks of which furnish a resin that is made into the violently toxic snuff called "yakee" or "paricá" by Indians of the northwest Amazon. Medicine men use yakee for prophesying or diagnosing disease, usually inhaling up to one heaping teaspoonful of the brownish gray powder. According to Schultes (53) whose paper of 1954 (54) is virtually the only reference on this exotic drug, the users then "fall into a delirious stupor or sleep during which the shouts they emit are interpreted by assistants. That the intoxication can be dangerous is admitted by the medicine men themselves, and the death of one medicine man of the Puinave tribe . . . is laid to the use of *yakee* snuff." Schultes notes (53) that the active principle of yakee "has not yet been determined, but there is every reason to believe it to be the same essential oil [*sic*]—myristicine—which occurs commonly throughout the family and which is the narcotic principle in household nutmeg."

In 1964, however, Holmstedt analyzed samples of *Virola* snuff for tryptamines and found 5-methoxy-N,N-dimethyltryptamine to be a major component of this narcotic. He also discovered small amounts of N,N-dimethyltryptamine (DMT) and 5-hydroxy-N,N-dimethyltryptamine (bufotenine) (66). The pharmacology of 5-methoxy-N,N-dimethyltryptamine is poorly understood, but both DMT and bufotenine are known psychotomimetic drugs.

Even these meager data on *Virola* are more conclusive than almost anything yet available on the narcotic use of Myristica. The search for answers to the question: Is nutmeg used as a narcotic? leads to innumerable blind alleys. To begin with, the medical literature is of no help because nearly all the reported cases of nutmeg intoxication have resulted from accidental ingestions or from overdoses taken as remedies. Documented accounts of the deliberate use of Myristica for narcotic effects are discouragingly hard to find, and it is not surprising that the Federal Bureau of Narcotics writes (55): "The common nutmeg, *Myristica fragrans* is not considered to contain narcotic substances; and it therefore is not under the jurisdiction of this Bureau. We are not aware of any constituents of nutmeg which would bring it under the control of the Federal Narcotic Law, nor do we have any data concerning its use."

At the same time, there is an impressive amount of anecdotal material suggesting that nutmeg is consumed as a psychoactive agent by many people throughout the world. One hears persistent rumors, for instance, that Myristica serves as a narcotic in the Orient, that it is commonly taken by prison inmates, and that it has caught on as a new hallucinogen among bohemians. The remainder of this section is an appraisal of such rumors.

Is nutmeg used as a narcotic in the East? In 1883, Dymock (21) wrote that the Hindus of western India take Myristica as an "intoxicant"—not just as a broad-spectrum remedy and aphrodisiac. His brief reference is one bit of published evidence which supports the curious popular belief among American narcotics-users that nutmeg is in widespread use in India. Another scrap of confirmation is a second line from Dymock, in a paper of 1889, "The Spices and Drugs of the East" (2): "Nutmegs are narcotic and are often eaten with *pan supari.*" But nowhere else in Indian medical literature is Myristica spoken of in connection with *pan* (betel chew) except as a flavoring adjunct. In addition, most native students of Indian customs are unaware of the narcotic effects of the spice. Finally, with the abundance of hemp preparations available in India, one would not expect the people of that country to have to resort to Myristica.

Yet, there is reason to believe that Indian folk practices embrace the use of nutmeg as a narcotic, though certainly not on as wide a scale as drug-takers in this country seem to think. An obscure clue is one of the synonyms for nutmeg used in Ayurveda: *Mada shaunda,* meaning "narcotic fruit." Dr. C. Dwarakanath of the Indian Ministry of Health informs me (23) that "*M. fragrans* is generally chewed together with betel for the slight excitement is gives. It is also consumed orally with a view to stimulating the libido. *Mada shaunda* refers to its narcotic action." He adds that "in certain parts of southern India, *M. fragrans* is mixed with tobacco snuff and used." K. R. Ramanathan of the Council of Scientific and Industrial Research, New Delhi, has tried to get more information on this last implication. He writes (23): "We have made some inquiries regarding its use in the manufacture of snuff, where it is reported to be employed as one of the ingredients. While the large-scale manufacturers have denied the use of nutmeg in snuff manufacture, it is possible that nutmeg may be used on a very restricted scale by those who are aware of its properties." Evidently, there is some factual basis to the rumored consumption of nutmeg as a narcotic in India.

Another story frequently encountered is that *Cannabis* devotees will turn to nutmeg when they cannot get hemp. Again, there is only one bit of supporting evidence—a line from Bamford's *Poisons* (15) of 1951: "Within the last few years, partly owing to the difficulty in obtaining hashish, it has become the practice in Egypt to substitute powdered nutmeg. In sufficiently large doses this produces symptoms similar to those of hashish intoxication and the effects may even be much more severe." Unfortunately, governmental agencies in Egypt have not answered questions about this practice, and no other writer confirms Bamford's observation. An Israeli pharmacologist comments (19): "I have not come across any use of *Myristica fragrans* as a narcotic among the Arabs in Israel, but that does not mean to say that there is not some use of it for that purpose." Regrettably, the matter must be left there.

A final implication of Myristica as a narcotic in the East is its rumored use as a snuff in Indonesia and Malaya. Klaus Stopp, who spent much time in the area, says (56) that "no use of nutmeg as a narcotic had come across to me in New Guinea; if there is such a use in the Eastern part, it must be very local." On the other hand, Nathan S. Kline, on returning from Indonesia in 1964 wrote (57): "It is my understanding that nutmeg is often used as a snuff during attendance at the Wayang plays which often go on from early in the evening until the next morning." The Wayang plays are kinds of puppet shows, popular throughout much of southeast Asia; no confirmation of Kline's belief is yet available. In fact, two independent investigators in Indonesia assure me that nutmeg is *not* used as a narcotic in that country, except possibly in very rural eastern areas (58).

Is nutmeg used as a narcotic in prisons? Most stories in circulation about nutmeg as a narcotic concern its use in prisons. If they are true, it would seem that nutmeg and mace could often be serious problems in correctional institutions. An officer of the Federal Bureau of Prisons dismisses this idea as an exaggeration (59):

> We are aware of the narcotic reaction these spices may have when improperly used, and therefore, it is standard practice in the Federal prisons to maintain careful control of both items. Due to this control and also to the fact . . . that few people are aware of their stupor-inducing powers, we have no problems with these items. I have read articles in various publications which imply that the use of nutmeg and mace is widespread in prisons. However I do not know of a single instance in the Federal Prison system where either spice was used by inmates for its narcotic effect.

But his statement does not settle the issue. A short article on page 22 of the Chicago *Sun-Times* of March 3, 1961, headlined "Nutmeg Costs a County Jail Guard His Job," proves at least that people in some prisons know what Myristica can do. The article begins: "A County Jail guard was fired Thursday (March 2, 1961) after he was caught trying to help inmates get a cheap thrill. Warden Jack R. Johnson said Robert H. Brooks, 49, was apprehended Wednesday taking nutmeg and nose inhalers into the jail. Brooks . . . had four ounces of nutmeg and 16 inhalers suspended inside his trousers, Johnson said." The writer did not bother to explain what sort of "cheap thrill" one can get from nutmeg and nose inhalers.

More evidence comes from the Director of the Addiction Research Center at the United States Public Health Service Hospital in Lexington, Kentucky—W. R. Martin. Martin (60) says that many patients he has seen believe mace and nutmeg, especially nutmeg, to have "stimulating effects," usually because they have heard the prevalent rumors. He adds that patients rarely volunteer information on Myristica experiences and that the practice of using nutmeg or mace is far from universal; but he estimates that about one out of ten Lexington patients will admit having tried occasional self-experiments with these spices. Most persons who have used Myristica, he feels, do not attach much importance to it until they are confined within instiutions. Martin also writes:

> I spoke this morning with . . . the chief of security at this hospital. . . . To his knowledge there has never been any incidence of acute intoxication with either of these agents in the hospital. He believes that the use of these agents may be more common in prisons in which the main population is made up of addicts, than in general prisons. Although there have been no cases of reported intoxication, he said the effects of these agents on the prison community are very similar to those of heroin and barbiturates. Gangs are organized to sell them, and fights and disorders may result when a customer fails to pay off his obligation.

There is substantial confirmation of Martin's impressions in an article by Weiss (61) describing a study on the "Hallucinogenic and Narcotic-like Effects of Powdered Myristica" conducted at the New Jersey State Prison, Trenton, in 1960. Weiss notes that many commercial and medicinal substances are used covertly by prisoners to "escape from one's self and the depressing, immediate surroundings," and he says without qualification: "Powdered myristica . . . is included among the inmates' repertory of alleged euphoria-inducing drugs."

> It is widely believed by inmates of correctional institutions that the drug action of nutmeg produces reactions similar to those of legally prohibited drugs which are considered habit forming and addicting. Although its illicit application is most certainly not widely known in the extra-mural setting, personal communications by prisoners are to the effect that it is used, not only in the community [i.e., the outside], but was also used in the armed forces in Europe in World War II.

Weiss studied ten male inmates of the prison, most of whom had had previous experience with marihuana and other drugs. Six of them had learned of the use of nutmeg during their imprisonment; the others had already known about it. He obtained introspective reports "chiefly from eight subjects, since two developed toxic psychoses as a result of chronic ingestion of ground nutmeg." The first astonishing fact Weiss uncovered was the frequency with which some prisoners use Myristica. Of his ten subjects, one had tried nutmeg 10 different times, one 30, one 52, and one 475.

Equally interesting are the dosages and reactions. The minimum amount of ground nutmeg any man ingested was two to three tablespoonfuls, and one had once taken *two cups* of the spice as a single dose (apparently without unusual reactions or permanent systemic damage). The drug was always taken orally, usually stirred into hot liquids (61):

> The effects of these large dosages differ substantially from those cited by Power and Salway. While some of the inmates experienced drowsiness, none experienced stupor or delirium. No uniformity was reported with respect to the onset of effects, which ranged from 10 minutes to four hours, and with respect to the duration of action, which ranged from a minimum of four to five hours to a maximum of 24.

Most of the subjects compared nutmeg to marihuana. One said: "It made me feel light, like with a marihuana cigarette" though another explained: "One reefer will get you three times as high as nutmeg; it slows your actions down."

Weiss concludes that:

> Doses of two to three tablespoonfuls of powdered nutmeg tended to narcotize the subjects against the unpleasant experience of incarceration, without a blurring of the boundaries between the self and the outer world. The effects were considered to be essentially similar to those of marihuana, although comparisons with heroin and alcohol were also cited. In most instances, a feeling of being transported aloft was experienced accompanied by a feeling of drowsiness in some cases and excitement or stimulation in others. . . .
>
> Symptoms of physiological addiction were not reported. No positive correlation was obtained between the 'light-feeling' and the mood experience. Nor did the mood experience, be it gay or melancholy, for example, serve as an index as to whether inmates would prefer to promote social contacts or encyst themselves from them. It was also reported, in most instances, that the ability to enjoy certain pastimes was enhanced. In all instances of recall, thirst was increased, and hunger was largely diminished or unaffected. The various side effects reported were nausea, abdominal spasm, vomiting, constipation, tachycardia, insomnia, and drowsiness.
>
> Two cases of acute brain syndrome, with psychotic reaction due to nutmeg intoxication, were reported. Each of the two subjects had chronically ingested powdered nutmeg over a long period. . . . Aside from the cases of nutmeg poisoning, the hallucinogenic effects reported were transitory and of brief duration.

Nutmeg has since been banned from the New Jersey State Prison kitchen, but Weiss has continued to gather facts on its use. He adds the following notes (62):

> Inmates in the past [i.e., before the ban] would carry little match boxes in which they would store a supply of nutmeg (equivalent to one dose). They could then take the dose along with them to the shops in which they worked during the day. Users consider themselves to be more lively and cheerful. Thus, they feel they have dispelled their inner gloom. However, drug users seldom take nutmeg once they leave the prison since they consider its effects to be inferior to those of heroin or marijuana, whatever may be the similarity between them.

Weiss's article leaves no doubt about the use of Myristica in American prisons, despite the statement of the Federal Bureau of Prisons. Further information comes from an informant who was recently an inmate at a state prison. He writes:

> During 16 months in a Massachusetts correctional institution, I knew three individuals who on occasion did use nutmeg as a snuff for 'kicks.' It was done only on weekends and widely dispersed as to time. At Synanon in California [a self-help addicts rehabilitation center] both nutmeg and mace have been used, but it is not a common problem. Two or three residents tried both nutmeg and mace while I was there. It was not considered Kosher by the Synanon family, it was considered a 'Mickey-mouse' deal, ridiculed rather than disciplined otherwise. There seems to be little history of the use of nutmeg or mace among prisoners other than addicts. I suspect it is because other drugs can be obtained too easily, even within correctional structures. The correctional officers admit to the validity of this statement.

Enoch Callaway, one of Truitt's co-workers, suggests (63) that officials know very little about nutmeg, because prisoners almost never admit to using it. Callaway also believes that large spice companies know much about the possibilities of nutmeg and mace but "pretend they don't." It is certainly true that most large processors of spices deny knowledge of Myristica's effects; according to Callaway, however, "they have to guard every shipment of mace and nutmeg they get," in order to keep them from being stolen by persons who consume them regularly.

Do bohemians and students use nutmeg as a narcotic? A Harvard undergraduate gives me the following information:

> I recently received a visit from a beatnik acquaintance who smokes marihuana frequently and has tried other drugs. I mentioned to him that I knew someone who was writing about nutmeg as a narcotic, and he said, "We've known about that for years." He explained that he and many of his friends had tried nutmeg several times, taking it both as a snuff and by mouth. They did not think it was very good, however, because "you either get very sick or have a horrible experience." He said that people who like to "blow pot" [i.e., smoke marihuana] sometimes take nutmeg when they can't get their usual drug. He told me nutmeg was much used in India.
>
> We happened to be in the kitchen, and my friend took me over to a spice cabinet. "Nearly everything in there will get you high," he said, "except for monosodium glutamate." He told me he occasionally smoked cinnamon sticks for their drug effect, and he recommended smoking paprika "if you want to have a powerful experience." He was afraid to try ginger, though, because he had heard it could be dangerously potent.

These startling capabilities of familiar substances are plausible, since all aromatics contain volatile compounds which affect the central nervous system. What is most interesting is the way each drug comes to offer a different experience to the narcotics-user—nutmeg can be "horrible," for example, or ginger "dangerously potent." Here is an illustration of the influence of psychological set on the drug experience. A person expecting horrible effects from nutmeg will probably get them. Likewise the reason prisoners in New Jersey had predominantly pleasant times with Myristica is probably that they expected nutmeg to help alleviate the boredom of prison.

A great many young people today expect (and get) "mindbroadening" experiences from a number of substances: the true hallucinogenic drugs, marihuana, morning glory seeds, airplane glue, certain cough syrups,[4] and others. Is nutmeg on the list?

Callaway (63) maintains that jazz musicians "have been on to nutmeg for some time" but warns that they will not discuss it, except with people they know well. The same probably applies to most bohemians, addicts, and students who try out the spice; but if the rumors on these uses are also true, large numbers of young Americans have experimented, at least once, with nutmeg or mace. Very likely, most do not come back for a second try. Both spices are quite difficult to get down in the necessary amounts and nearly always cause a rash of unpleasant symptoms, even when they do produce pleasant changes of consciousness.

Payne's report (45) of 1963 is the only case of this type reported in the scientific literature. The two college men whom he examined had each taken two tablespoonfuls of powdered nutmeg in a glass of milk. "This procedure had been recommended by a 'beatnik' acquaintance as providing a mental state somewhat akin to ethanol intoxication without requiring the use of alcohol."

Experimentation with nutmeg may be widespread on American campuses. For example, in 1964, in the summer issue of a University of Mississippi student magazine there appeared an article titled "Nutmeg Jag," describing a nutmeg party attended by eight persons. One participant—a young man who consumed a whole standard-size can of the ground spice—reported afterward (64): "I felt as if I were in an echo chamber . . . my voice sounded vague and distant . . . it was like being drunk without the ordinary alcoholic effects. . . . Two friends of mine had told me about the 30-cents three-day drunk they had after taking nutmeg, so I tried it out of sheer disbelief." All of these nutmeg-eaters suffered extreme physical discomforts as a result of their party.

Probably most students who try nutmeg

---

[4] Romilar's CF cough syrup, available without prescription, is the latest item to receive wide publicity as a psychedelic agent. It has been used especially by college students to induce euphoria and bizarre mental states. The syrup is sold in 3-ounce bottles, and one is told to drink 4 ounces to "turn on." Use of Romilar's has come to the attention of several physicians, who say that there is no pharmacological basis for these claims.

take it out of curiosity and do not come back for more than one intoxication. I have collected the following accounts from three students at eastern colleges:

1. "I heard about the effects of mace from a beatnik who visited our campus and induced a number of students to 'turn on' with two teaspoons of this spice stirred into water. (He did not mention nutmeg, by the way.) I didn't try it at the time, but a few months later five of us held a 'mace party' in my apartment. To the disappointment of all, we felt just the same three hours after drinking down the mace. Convinced that the alleged hallucinogenic properties of mace were imaginary, we separated and I went home to bed. I remember feeling somewhat lightheaded and having vague stomach pains before falling asleep, but I had no other symptoms until I woke up the next morning with a splitting headache, a burning thirst, and malaise. I later learned the other four had felt much the same on arising." 2. "A friend told me mace would cause visions, and I decided to try it. I had taken mescaline a few weeks before and liked that very much, especially the brilliant color visions. So I mixed two teaspoons of ground mace with fruit juice and swallowed it. A few hours later I began seeing visions when I closed my eyes—like those with mescaline but not nearly as intense. I was thirsty and lethargic all the next day and had a bad headache. I have no desire to repeat the experience." 3. "Five of us tried to get high by eating two whole nutmegs each. They are terrible things to try to chew up and swallow. We all had warm feelings in our stomachs immediately afterward and began sweating more than usual. One of us eventually had a pronounced reaction, but the rest of us noticed nothing unusual and gave up. The next morning we all had headaches, extreme dryness of throat and mouth, creaking joints, and dizziness. We felt just awful. One of us, however, had a different experience. He went back to his room to read, and exactly four hours after taking the nutmeg, he was suddenly overcome by a drowsiness so profound that he could hardly get up to turn off the light. As he fell into bed, he saw or had impressions of 'strange shapes floating' around him. He then sank into a heavy sleep from which he awakened seven hours later to find that he could barely move. He was very dizzy and staggered when he tried to walk; also, he could not see clearly for several minutes. His mouth and throat were parched, and no amount of water he drank relieved the dryness. Two hours after he got up he again became drowsy and 'sank into a sort of trance state.' During this time he had a vivid impression that he was floating with his limbs separated from his body. Eight hours later, he was completely recovered."

As a final word on the use of nutmeg, there is the report of Truitt et. al. (51) that the practice of taking this plant product to produce "a syndrome comparable to alcoholic inebriety" is "not uncommon among alcoholics who are deprived of alcohol."

Psychopharmacology of Nutmeg: A Brief Note

Speculation on the psychopharmacology of nutmeg must be cautious, since, as Shulgin says (52), "the inability to assign to a single component of nutmeg the role of being the toxic factor makes a discussion of the mode of action, by definition, totally theoretical."

Nonetheless, a few findings are interesting. Truitt and a new group of researchers published a paper (65) in 1963, for example, which pointed out "a degree of structural resemblance between the chemical formula for myristicin and those of certain sympathomimetic amines." This similarity, together with nutmeg's stimulating action, suggested that myristicin and nutmeg may act as central monoamine oxidase (MAO) inhibitors. To test this hypothesis, synthetic myristicin and nutmeg oil concentrate were given to rats, and MAO inhibition was established by measurement of potentiation of tryptamine convulsions. Controls were run with two potent known MAO inhibitors, tranylcypromine and iproniazid. By these methods, myristicin was shown to produce effects less potent than but parallel to those of the reference drugs. Myristicin was also found to antagonize reserpine ptosis and to increase brain 5-hydroxytryptamine—both of which are changes induced by other MAO inhibitors.

The authors emphasize that this is mere

circumstantial evidence, but they feel that nutmeg and myristicin are probably mild MAO inhibitors. Compared to other such compounds, their toxicity is quite low. The authors cite preliminary work with schizophrenic and depressed patients in which daily administration of ground nutmeg caused definite improvements. They conclude: "Further study is recommended for more direct evidence of nutmeg and myristicin as enzyme inhibitors and for their utility as anti-depressant drugs."

Shulgin, who has been concerned with the biochemistry of nutmeg's hallucinogenic action, assumes (52), for the moment, that the myristicin fraction of the oil (with its more than 25 per cent content of elemicin) is, indeed, the active principle. He notes that the metabolism of the aromatic ethers found in essential oils is "virtually unknown," except for a detoxication mechanism by which safrole is converted to piperonylic acid. This reaction indicates a capacity to oxidize an olefinic side chain. Shulgin suggests that, if this degradative process is "applicable to myristicin, or especially to elemicin, a theoretical intermediate, a vinyl alcohol, could undergo transamination producing the known psychotomimetic drug, 3,4,5-trimethoxy amphetamine (TMA). The recent description of the new, synthetic hallucinogen—3-methoxy-4,5-methylenedioxy amphetamine (MMDA)—which might be derived by an analogous process from myristicin, itself, is even more suggestive of a psychotropic function for this component of nutmeg (see Fig. 2) (16).

Thus far, human pharmacological data are inadequate to support the contention that myristicin is psychoactive or that it is an active principle of whole nutmeg. Shulgin concludes (52): ". . . some combination of factors in total nutmeg is capable of producing a psychotropic response: the structure of elemicin or myristicin wanting only an ammonia molecule to become a recognized mental agent must be accepted as at least an intriguing coincidence."

Conclusions

The seeds and arils of *M. fragrans* have powerful narcotic properties. In man, they have frequently caused serious but almost never fatal intoxications. Most Westerners are ignorant of these toxic properties and know nutmeg and mace only as flavoring agents.

Both spices are used as narcotics, probably by significant numbers of people, although information on this use of Myristica is scarce. When taken deliberately as psychotropics, nutmeg and mace often cause reactions quite unlike those described in classical accounts of Myristica poisoning and much more like typical hallucinogenic drug experiences.

Thorough investigations of the history, sociology, and biochemistry of Myristica narcosis would be valuable from many points of view.

References

1. Huxley, Aldous. The Doors of Perception, New York: 1954.
2. Ferguson, A. M., and J. Ferguson, All About Spices, Colombo, Ceylon: 1889.
3. Ridley, Henry N. Spices, London: 1912.
4. Warburg, O. Die Muskatnuss, Leipzig: 1897.
5. de Ebulo, Petrus. Carmen de motibus siculis ca. 1195.
6. Masudi, Les Praires d'Or, 9th Century, (published at Paris in translation by Barbier and Meynard).
7. Redgrove, H. Stanley. Spices and Condiments, London: 1933.
8. Cardullo's Delicatessen, Cambridge, Mass.
9. John Wagner & Sons, spice dealers: label on container of nutmeg.
10. Guenther, E. The Essential Oils, 1952.
11. John Wagner & Sons, spice dealers: label on container of ground mace.
12. Power, F. B., and A. H. Salway. The constituents of the fixed oil of nutmeg. Jour. Chem. Soc. **93:** 1653-1659, 1908.
13. The Pharmacopoeia of the United States of America. XV, Easton, Pa., 1955.
14. Power, F. B., and A. H. Salway. The constituents of the essential oil of nutmeg. Jour. Chem. Soc. **91:** 2037-2058. 1907.
15. Bamford, F. Poisons, 3rd rev. ed., Philadelphia: 1951.
16. Shulgin, Alexander T. The possible implication of myristicin as a psychotropic substance. Unpublished paper, October, 1964.
17. Shulgin, Alexander T. Composition of the myristicin fraction from oil of nutmeg. Nature **197:** 4865, January 26, 1963, p. 379.

18. Ainslie, W. Materia Indica, London: 1826.
19. Zaitschek, David V. School of Pharmacy, Hebrew University, Jerusalem, quoted by Asaph Goor, Ministry of Agriculture of the State of Israel, Jerusalem, in personal communication, January 20, 1964.
20. von Martius, K. F. P. Beitr. z. Litteraturgesch. d. Muskatnuss u.d. Muskatbl. 1860.
21. Dymock. Materia Medica of Western India. Bombay: 1883.
22. Burkill, I. H. A Dictionary of the Economic Products of the Malay Peninsula, London: 1935.
23. Dwarakanath, C. Adviser on Indigenous Medicine, Ministry of Health, Government of India; quoted by K. R. Ramanathan, Senior Scientific Officer, Council of Scientific and Industrial Research, New Delhi, personal communication, June 18, 1964.
24. Parkinson, John. Theatrum Botanicum. London: 1640.
25. Green, Robert C., Jr. Nutmeg poisoning. Jour. Amer. Med. Assoc. **171**(10): 1342–1344. 1959.
26. McCord, J. A., and L. P. Jervey. Nutmeg (Myristicin) poisoning. Jour. S. Carolina Med. Assoc. **58**(1): 436–438. 1962.
27. The Dispensatory of the United States of America, XXV. Philadelphia: 1955.
28. The Wealth of India: Raw Materials, Vol. VI. New Delhi: 1962.
29. Bontius, J. De Medicina Indorum. Leyden: 1642.
30. Regel, K. Das mittelniederdeutsche Gothaer Arzneibuch und seine Pflanzennamen. Osterprogr. des Gymnas. Ernestin zu Gotha, 1873 (quoted in Warburg, op. cit.: 575).
31. Cullen, William. A Treatise on the Materia Medica. London: 1789.
32. Hanzlik, P. J. Purkinje's pioneer self-experiments in psychopharmacology. California and Western Medicine **49**(1): July, 1938 and Aug., 1938.
33. Purkinje, J. E. Einige Beitraege zur physiologischen Pharmacologie. Neue Breslauer Sammlungen aus dem Gebiete der Heilkunde **1**: 423–443. 1829. (quoted in Hanzlik, op. cit: 141).
34. Endlicher. Enchiridion bot.: 421. 1841. (quoted in Warburg, op. cit.: 567).
35. Pereira. Materia Medica, 3rd. ed., 1836. 1850 (quoted by Warburg, op. cit.: 567).
36. Watson, G. C. Symptoms of poisoning after eating a quantity of mace. Prov. Med. Surg. Jour. January 26, 1848 (read before the Liverpool Medical Society, 1847 .
37. The Dispensatory of the United States of America, XIX. Philadelphia: 1907.
38. Hammond, P. W. Nutmeg poisoning. Brit. Med. Jour. 1906–II: 778.
39. Farnsworth, P. J. *in* Squibb, Ephemeris of Materia Medica, etc., VII, 1904: 243–244.
40. Dale, H. H. Note on nutmeg poisoning. Proc. Royal Med. Soc. 1908–1909–II: (discussion) 74.
41. Beck, R. Muenchen Med. Wschr. **61**: 878. 1914.
42. Alexander J. Poisoning by nutmeg. Brit. Med. Jour. 1887–I: 1085; Bartlett, B. F. Nutmeg poisoning, Brit. Med. Jour. 1911–II: 269; Bentlif, P. B., Case of poisoning by nutmeg. Brit. Med. Jour. 1889–II. 1389; Carvell, G. H., Poisononing by nutmeg. Brit. Med. Jour. 1887–I: 1317; Gibbins, K. M., Nutmeg poisoning. Brit. Med. Jour. 1909–I: 1005; Hamilton, J. Nutmeg poisoning. Brit. Med. Jour. 1906–II: 900; Johnson, J. nutmeg poisoning. Brit. Med. Jour. 1906–II: 984; Pitter, R. A. A case of nutmeg poisoning. Lancet. 1902–I: 1035; Reekie, J. S. Nutmeg poisoning. Jour. Amer. Med. Assoc. **52**: 62, Jan. 2, 1909; Simpson, T. G. Case of poisoning by nutmeg. Lancet 1895–I: 150; Smith, S. M. Nutmeg poisoning. Lancet 1902–I: 1798; Wilkinson, A. N. Poisoning by nutmeg. Brit. Med. Jour. 1906–I: 539; and Wilkinson, K. D. Nutmeg poisoning. Brit. Med. Jour. 1911–I: 993.
43. Cushny, A. R. Nutmeg poisoning. Proc. Royal Soc. Med. 1908–I(3): 39.
44. Mendelsohn, G. Two cases of poisoning by nutmeg. Deutsch. Med. Wschr. **33**: 2001. 1907.
45. Payne, Robert B. Nutmeg intoxication. New Eng. Jour. Med. **269**(1): 36–38. 1963. (Mention of this article was made a few weeks later in the "Medicine" section of TIME Magazine.)
46. Mitscherlich. Lehrbuch der Arzneimittellehre, 2nd. ed., 1849 (cf. Warburg, op. cit.: 568).
47. Wallace, G. B. Contributions to Medical Research. Ann Arbor: 1903.
48. Jurss, F. On myristicin and some closely related substances. Bericht of Schimmel and Co., Leipzig: 1904.
49. Power, F. B., and A. H. Salway. Chemical examination and physiological action of nutmeg. Amer. Jour. Pharm. **80**: 563–580. 1908.

50. Truitt, Edward B. et al. The pharmacology of myristicin: a contribution to the psychopharmacology of nutmeg. Digest of Neurol. Psychiat. **29**: 274. 1961.

51. ———. The pharmacology of myristicin: a contribution to the psychopharmacology of nutmeg. Jour. Neuropsychiat. **2**(4): 205–210. 1961.

52. Shulgin, Alexander T. Concerning the pharmacology of nutmeg. Mind. Oct., 1963: 299–303.

53. Schultes, Richard E. Hallucinogenic plants of the new world. Harvard Rev. **1**(4): 18–32. 1963.

54. ———. A new narcotic snuff from the northwest Amazon. Bot. Mus. Leaflets, Harvard University **16**(9): 241–260. 1954.

55. Siragusa, Charles. Deputy Commissioner of Narcotics, United States Bureau of Narcotics. Personal communication, April 8, 1963.

56. Stopp, Klaus. Institut für Spezielle Botanik and Pharmakognosie der Universitaet Mainz. Personal communication, January 22, 1964.

57. Kline, Nathan S. Director of Research, Rockland State Hospital, Orangeburg, New York. Personal communication, February 10, 1964.

58. Setyonegoro, K. Department of Psychiatry, University of Indonesia, Djakarta, Indonesia; A. J. Kostermans, Herbarium Bogoriense, Bogor, Indonesia.

59. Alldredge, Noah L., Deputy Assistant Director, United States Bureau of Prisons. Personal communication, April 6, 1964.

60. Martin, William R., Director, Addiction Research Center, United States Public Health Service Hospital, Lexington, Kentucky. Personal communication, April 9, 1964.

61. Weiss, George, Hallucinogenic and narcotic-like effects of powdered myristica (nutmeg). Psychiat. Quart. **34**:(1): 346–356, 1960.

62. ———. Personal communication, April 18, 1964.

63. Callaway, Enoch. Chief of Research, The Langley Porter Neuropsychiatric Institute, San Francisco, California. Personal communication, April 6, 1964.

64. Andre, Sigrid. Nutmeg jag. Mississippi Mag. **4**(1): 18. 1964.

65. Truitt, Edward B. et al. Evidence of monoamine oxidase inhibition by myristicin and nutmeg. Proc. Soc. Exp. Biol. Med. **112**(3): 647–650. 1963.

66. Holmstedt, Bo. Tryptamine derivatives in *epená*—an intoxicating snuff used by some South American Indian tribes. Arch. int. Pharmacodyn. *in press*. 1965.